* Flow through the arterioles and the state of the precapillary sphincters dictates capillary flow
* The intercellular cleft is fenestration in capillaries filled with water so water soluble things can go through if they are small enough (albumin is too big) 🡪Intracellular movement
* Caveolae (plasmalemmal vesicles)
  + Transcellular movement --Used by myoglobin
* Solute exchange across tissue capillaries is by diffusion
  + Related to:
    - Their concentration gradient
    - Permeability of the capillary wall
    - SA of capillary wall
    - MW (bigger diffuse more slowly)
    - Distance (↑ dist the longer it takes to diffuse)
    - Charge of the solutes moving across (neutral and + charge move relatively easy)
    - Lipid vs. water soluble molecules –more
* Water movement across the capillaries is by convection and is dependent upon a balance of hydrostatic (P in capillaries forcing water out) and osmotic pressures (P pulling water back in) across the capillaries
  + Why doesn't water diffuse from capillaries into interstitium? B/c osmolality is the same in all compartments!
  + Osmotic pressure/oncotic pressure is related to proteins in the blood and Proteins attract water
  + In the capillaries closer to the arteriolar side you get net filtration of water and near the venous side you get net reabsorption of water b/c as you get close to the venous side
    - Most of the filtered fluid at the arteriolar end is reabsorbed at the venous end
* Absolute capillary pressure tends to follow venous pressure when resistance on each is unchanged
  + R veins < R arterioles so Rv/Ra would be a fraction
  + Arterioles are upstream of capillaries and veins are downstream of capillaries
  + Arteriolar dilation or venoconstriction will ↑ capillary P
  + Arteriolar constrction or venodilation will ↓ capillary P
  + If you stand too long Pv ↑ so Pc ↑ and a high Pc causes water to filter out leading to edema (Edema= clinically apparent ↑ in the interstitial fluid volume )
* Things that cause Edema
  + CHF b/c of ↑ volume retention🡪 ↑ vascular fullness so blood is stored in the veins🡪↑ Pv🡪 ↑ Pc🡪 edema
  + ↓ in proteins so ↓ in reabsorption of water (↓ in plasma colloid osmotic pressure/oncotic P)
    - Hepatic cirrhosis, Malnutrition, Nephrotic Syndrome, Catabolic state
  + Prolonged erect posture or DVT
    - ↑ ↑ in Pv🡪 ↑ ↑ in Pc 🡪 edema

**O2 Consumption**

* Metabolically active tissues reduce hemoglobin’s affinity for O2

**O2 Extraction**

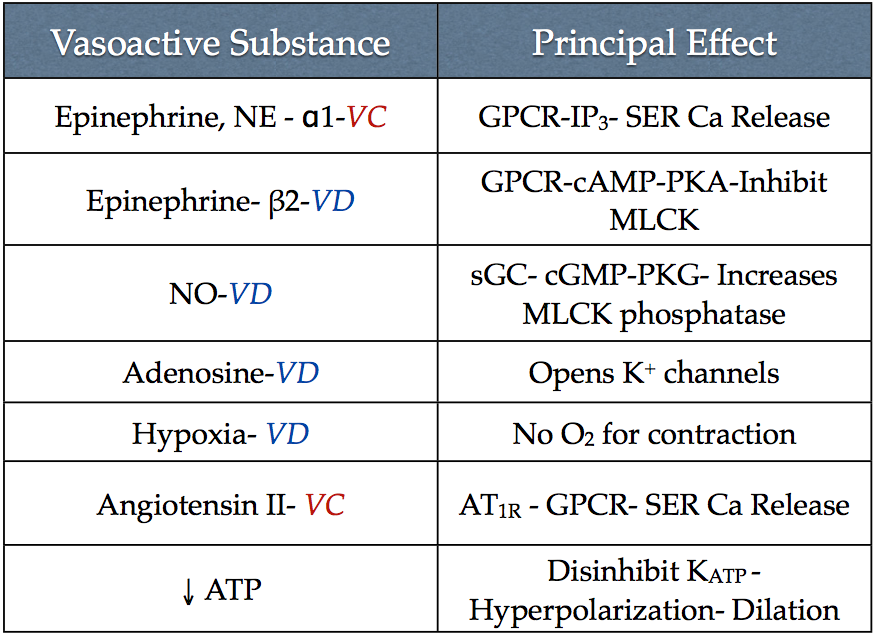
* Regular resting tissues extract ratio is only 25%; Heart extracts like 80% so its very prone to ischemia
* In ↑ O2 demand/ Tissue metabolic consumption can ↑ Flow or ↑ Extraction

**To regulate flow**

* ↑ SNS tone🡪 vasoconstriction🡪 ↓ flow
* ↓ SNS tone🡪 vasodilation 🡪 ↑ flow
* \*local arteriolar SM constriction or dilations controls tissue flow

**To regulate extraction**

* Metabolically active tissues have ↑ CO2/↑ H+/↑ 2,3-DPG; all of these things ↓ Hg affinity for O2 so more O2 is released and you have ↑ extraction
* Arterial vasodilation fails to tx myocardial ischemia post MI why? B/c the arteries are already dilated b/c if heart wants to ↑ O2 supply they are already at max extraction so the body ↑ flow by vasodilation. A vasodilator like nitroglycerin will have no effect.
* Organs control their local blood flow dependent on metabolic need
* SMC contract with intracellular calcium ↑
  + Voltage dependent calcium channels (L-type) open during depolarization (PM getting more +) and let in extracellular calcium
    - Opening of these ↑ vascular tone
    - These trigger intracellular ca to be released
  + **Ligand gated calcium channels** are receptor operated and are located on the sarcoplasmic reticulum
    - Respond to agonist –mostly epinephrine
    - Epinephrine binds to an α1 receptor (GPCR) on the PM and the IP3/DAG pathway signals the LGCC to release Ca2+ form SR (this is essential for contraction!)
  + MLCK
    - Activated by Ca2+/Calmodulin
    - Inactivated by PKA
  + MLC
    - When P’ed by MLCK (when it is P’ed once or de-P’ed by phosphatase) the SMC contract🡪vasoconstrict
    - When MLC is de-P’ed (inactive MLCK-- de-P’ed by phosphatase (which is activated by NO) or double P’ed by PKA) the SMC relax🡪 vasodilation
      * Vasodilation also occurs with ↓ intracellular calcium
  + Membrane polarity is determined by activity of K+ channels.
    - Changes in membrane polarity change activity of Ca channels
    - Open K channels🡪 ↑ K efflux 🡪 hyperpolarization 🡪 inact. L type CC 🡪 ↓ intracell Ca🡪 vasodilation
    - Closed K channels🡪↓ K efflux 🡪 depol 🡪 active. L type CC 🡪 ↑ intracell Ca🡪 vasoconstrict



* When tissues are metabolically active they consume ATP🡪 ADP🡪 AMP🡪adenosine🡪opens K channels🡪hyperpol🡪close VDCC🡪VD